

In re Application of:
Paul F. Worley
Application No.: 10/518,941
Filed: November 21, 2005
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PATENT
Attorney Docket No. JHU1880-1

Amendments to the Claims:

Please amend claims 1, 3-7, 10-13, 15-17, 20, 21, and 24-30 as indicated in the Listing of Claims.

Please cancel claims 23 and 35-71 without prejudice or disclaimer.

The listing of claims will replace all prior versions, and listings of claims in the application.

Listing of Claims:

1. (Currently amended) A method of screening for activity of modulating agents of a Homer signaling pathway comprising:

i) contacting at least one protein or peptide having a proline-type Homer ligand consensus sequence in the presence of a peptidylproline cis-trans isomerase (PPIase) inhibitor with at least one test agent for a sufficient time to allow the components to interact;

ii) contacting the [~~protein or peptide of~~] components of step (i) with a Homer protein;

iii) determining whether binding between the at least one protein or peptide and Homer protein is increased or decreased as compared to the binding in the absence of the test agent, wherein increased or decreased binding between the at least one protein or peptide and Homer protein is indicative of [~~the presence of~~] a modulating agent for a Homer signaling pathway.

2. (Canceled)

3. (Currently amended) The method of claim 1, wherein as the concentration of the at least one agent increases, [~~decreased~~] decreasing binding of Homer protein to the at least one protein or peptide is indicative of the presence of a competitive Homer ligand.

4. (Currently amended) The method of claim 1, wherein [~~the determining~~] step iii)

further comprises immunoprecipitation of a complex between the Homer protein and the at least one protein or peptide.

5. (Currently amended) The method of claim 1, wherein the PPIase inhibitor shows a biphasic [~~affect~~] effect at separate concentrations.

6. (Currently amended) The method of claim 5, further wherein the PPIase inhibitor is present in at least two concentrations, wherein [~~at least~~] one concentration of the inhibitor does not inhibit Homer binding to the at least one protein or peptide and another concentration of inhibitor inhibits Homer binding to the at least one protein or peptide.

7. (Currently amended) The method of claim 6, wherein [~~the~~] modulation of Homer protein binding by the agent at the concentration of PPIase inhibitor which does not inhibit binding of the Homer protein is indicative of the presence of [~~an~~] a modulating agent of a Homer signaling pathway.

8. (Original) The method of claim 1, wherein the PPIase inhibitor is a rotamase inhibitor.

9. (Original) The method of claim 1, wherein the PPIase inhibitor is selected from the group consisting of FK506, cyclosporin A, and GPI-1046.

10. (Currently amended) The method of claim ~~[[7]]~~ 9, wherein the PPIase inhibitor is GPI-1046.

11. (Currently amended) The method of claim 1, [further comprising determining] wherein binding between the at least one protein or peptide and Homer protein is determined by an endpoint assay selected from the group consisting of modulation of Ca^{+2} signaling, modulation of PLC, modulation of Trp channels, modulation of MAP kinase, modulation of PBkinase, modulation of ion channels, modulation of IP3 channels, modulation of RYR channels, and modulation of growth factor dependent responses.

12. (Currently amended) The method of claim 1, wherein the at least one protein or

peptide and Homer protein are [~~comprised~~] in a cell or cell lysate.

13. (Currently amended) The method of claim 12, wherein the at least one protein or peptide and Homer proteins are [~~comprised~~] in a [[cell]] cell.

14. (Original) The method of claim 13, wherein the cell is a transformed cell.

15. (Currently amended) The method of claim 14, wherein the at least one [~~amino acid~~] protein or peptide or the Homer protein is a recombinant peptide or protein.

16. (Currently amended) The method of claim 15, wherein the recombinant at least one protein or peptide is encoded by a nucleic acid encoding a consensus protein or peptide as set forth in [~~accession numbers~~ NP005451, NP037434, AAB97097, NP004548, Q00900, NP003249, NP840084, P009086, Q9JLU4, NP113939, NP067708, Q9WV48, P97836, AAF61375, AAD29417, P000531, AAC50926, P10275, NP776901, NP003295, NP057263, NP000829 or BAA05891] SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, or SEQ ID NO:53.

17. (Currently amended) The method of claim 16, wherein the nucleic acid encodes a sequence as set forth in [~~accession number~~ NP005451] SEQ ID NO:31.

18. (Original) The method of claim 1, wherein the Homer ligand consensus sequence is a proline-type 1 Homer ligand consensus sequence or a proline-type 2 Homer ligand consensus sequence.

19. (Original) The method of claim 18, wherein the proline-type Homer ligand consensus sequence is set forth in SEQ ID NO: 4.

20. (Currently amended) The method of claim 1, wherein the at least one protein or peptide is a synthetic oligopeptide comprising at least 4 amino acid residues, but not more than 10

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amino acid residues, having ~~[[a]]~~ the consensus sequence as set forth in SEQ ID NO: 4.

21. (Currently amended) The method of claim 20, wherein the synthetic oligopeptide ~~[consists of die protein or peptide as]~~ is set forth in SEQ ID NO:5.

22. (Original) The method of claim 1, wherein the at least one protein or peptide is selected from a protein in the group consisting of synphilin, EF2kinase, p70, Notch 4, AGIE-BPI, cytosolic thymidine kinase, neuronal PAS domain protein 2, zona pellucida sperm binding protein 3 precursor, Shank family of proteins, ryanodine receptor (RYP), p82, androgen receptor, TrpCl, mGluR1a and mGluR5.

23. (Canceled)

24. (Currently amended) The method of claim ~~[[23]]~~ 1, wherein the PPIase is selected from the group consisting of FKBP family, cyclophilin family, and Pin family of PPIases.

25. (Currently amended) The method of claim ~~[[25]]~~ 1, wherein the PPIase is FKBP 52 or FKBP 12.

26. (Currently amended) The method of claim ~~[[26]]~~ 25, wherein the PPIase is FKBP52.

27. (Currently amended) The method of claim 1, wherein the Homer protein is a human protein.

28. (Currently amended) The method of claim 1, wherein the Homer protein ~~[as set form in the accession numbers]~~ is selected from the group of consisting of ~~[NP-004829, NP-004830, NP-004263, NP-671705, NP-445762, and NP-445761]~~ SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, and SEQ ID NO:58.

29. (Currently amended) The method of claim 1, wherein the Homer protein comprises ~~[point mutations]~~ conservative amino acid substitutions.

30. (Currently amended) The method of claim ~~[[29]]~~ 1, wherein the Homer protein is

[as] set forth in SEQ ID NO: 7.

31. (Original) The method of claim 1, wherein the modulating agent functions as a neuroprotective agent.

32. (Original) The method of claim 31, wherein the agent is effective for treating neurodisorders selected from the group consisting of peripheral neuropathies and neurological pathologies related to neurodegeneration.

33. (Original) The method of claim 1, wherein the modulating agent functions as an immunosuppressive agent.

34. (Original) The method of claim 33, wherein the agent is effective for treating a disorder selected from the group consisting of psoriasis, inflammatory bowel disease, adult respiratory distress syndrome, dermatitis, meningitis, encephalitis, eczema, asthma, skin hypersensitivity reactions, atherosclerosis, leukocyte adhesion deficiency, rheumatoid arthritis, systemic lupus erythematosus (SLE), diabetes mellitus, multiple sclerosis, Reynaud's syndrome, autoimmune thyroiditis, experimental autoimmune encephalomyelitis, Sjorgen's syndrome, juvenile onset diabetes, tuberculosis, sarcoidosis, polymyositis, granulomatosis, vasculitis, pernicious anemia, diseases involving leukocyte diapedesis, CNS inflammatory disorder, multiple organ injury syndrome secondary to septicemia or trauma, autoimmune hemolytic anemia, myasthenia gravis, antigen-antibody complex mediated diseases, and transplantations, including graft vs. host or host vs. graft disease.

Claims 35-71. (Canceled)